the presence of HTN (n=217, 52%) if the arterial pressure was >140/90 mm Hg and/or they were being treated for HTN, and tested serum IgG antibodies to cytomegalovirus, hepatitis A virus, C*hlamydia pneumoniae, Helicobacter pylori,* herpes simplex virus type 1 and type 2, as well as C-reactive protein (CRP) levels. Results: The prevalence of antibodies to hepatitis A virus or *Helicobacter pylori,* but not to others, was higher in the HTN than the non-HTN patients. These associations were significant even after adjustment for traditional risk factors. Adjusted OR with 95%CL was 1.59 (1.05-2.40) for hepatitis A virus and 1.75 (1.15-2.68) for *Helicobacter pylori* infection. In addition, increasing number of seropositivities (pathogen burden) was significantly associated with increasing HTN risk. The prevalence of HTN was 58% in the high pathogen burden group (>4 positive antibodies) compared with 45% in the low burden group (P<0.01). The pathogen burden remained a significant predictor of HTN after multivariate analysis (adjusted OR 1.60 with 95% CL 1.05-2.42). Interestingly, we found that elevated CRP levels (>0.5mg/dL) were also associated with HTN (adjusted OR 1.80 with 95% CL 1.12-2.87), and that elevated CRP levels combined with individual infections and pathogen burden increased the risk of HTN: adjusted OR with 95% CL was 3.09 (1.56-6.12) for hepatitis A virus, 3.68 (1.83-7.40) for *Helicobacter pylori*, and 3.15 (1.56-6.37) for pathogen burden. Conclusion: Our data suggest that infection plays a role in the development of HTN, and elevated CRP levels can increase the risk posed by infection in HTN.

Noon

1059-11 Venous Endothelium Dysfunction Is Also Presented in Hypertensive Patients

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Background: Endothelium dysfunction has been demonstrated in the arteries of hypertensive patients. Although veins and arteries produce nitric oxide, it is unknown if the formers are also impaired in the arterial hypertension. The aims of this study were: 1) To evaluate whether or not the hypertensive patients exhibit venous endothelium dysfunction; 2) To determine the relationship between endothelium dependent and independent vasodilation responses in venous and arterial systems in these subjects.
Methods: Sixteen patients with mild hypertension (SBP 145.8 +/- 8.8 mm Hg and DBP 98.3 +/- 4.8 mm Hg), out of medication and without other risk factor, and fifteen matched normotensive volunteers had the venous and arterial endothelial function evaluated, respectively, by the dorsal hand vein (DHV) and high resolution ultrasound (flow mediated dilation - FMD) techniques.
Results: The maximal dilation response (Emax), produced by acetylcholine (ACH) was consistently reproducible, allowing evaluating the venous endothelium dependent response. Hypertensive group had a marked reduction of Emax to ACh (54,9+/-10,8%) when compared to normotensive controls (Emax= was 85,2+/-27,0%). The flow mediated dilation responses were reduced in the hypertensive subjects compared to their controls (6.6+/1.3 versus 12.4+/-1.4 %, respectively). The responses to nitric oxide donors were similar in both groups tested by the DHV and FMD methods. By the analysis of the measurement method comparison data (Bland & Altman), the responses both techniques agreed in normotensive and hypertensive subjects.
Conclusion: Hypertensive patients had an attenuated endothelial-dependent response, indicating that the endothelium dysfunction observed in arteries is also present in the venous system.

Noon

1059-12 Sustained Upregulation of Inflammatory Cytokine and Its Receptor Genes Associated With Proteinase Activation in Abdominal Aortic Aneurysm: Results From Combined Study With cDNA Array and Real-Time Reverse Transcriptase Polymerase Chain Reaction Methods

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Background: In the development of aortic aneurym, inflammatory process plays a pivotal role in the vessel tissue degradation. Under these conditions, cytokines are known to serve as an essential mediator of inflammation, contributing to degenerating local tissue associated with or without aneurysm formation probably through the activation of proteinases. However, few data exist regarding which cytokines are important for proteinase activation associated aneurysm formation. Therefore, we analyzed gene expression levels of cytokines, their receptors and proteinases such as matrix metalloproteinase (MMPs) in abdominal aortic aneurysm (AAA) by cDNA array and real-time RT-PCR methods.
Methods and Results: Aortic samples from the maximally dilated and non-dilated (control) regions were obtained from 22 patients with graft replacement surgery for AAA. The ^{32}P-labeled cDNA probe mixture synthesized from 5 microgram total RNA with gene-specific primers was hybridized with 388 cytokine-related cDNA array. For 4 pairs of AAA and control, the signal intensities for each target cDNA normalized to GAPDH were compared. Overt upregulation in AAA was observed for Interleukin (IL)-8 and its receptor such as CXCR-2, which were further confirmed by real-time RT-PCR method. We also determine gene expression level of MMP-1, 3, and 9. The expression levels for the IL-8 and CXCR-2 genes were significantly upregulated in AAA compared with control as followed: IL-8, 0.53 ± 0.16 Versus 0.11 ± 0.04 (p<0.01); CXCR-2, 2.04 ± 0.75 Versus 0.29 ± 0.10 (p<0.01). Under these conditions, there was significant upregulation of MMP-1 (4.48 ± 2.01 Versus 0.26 ± 0.12, p<0.01) and MMP-3 (5.01 ± 0.97 Versus 1.89 ± 1.00, p<0.05) genes.
Conclusion: Sustained upregulation of IL-8, a CXC-chemokine, and its receptor, CXCR-2, was observed in the AAA associated with overexpression of MMPs, suggesting that inflammatory process with proteinase activation contributes to the development of AAA. This pathway may be an alternative gene or drug target for the treatment of AAA.

Noon

1059-13 Detection and Propagation of Calcified Nanostructures From Human Aneurysms

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Background: Mechanisms leading to vascular calcification remain incompletely understood. Nanometer-sized, mineralized structures recognized by a commercially available monoclonal antibody (8D10, Nanobac OY) are present in calcified human aneurysms. These structures were not detected by TUNEL staining, suggesting they were not apoptotic bodies. The 8D10 antibody is directed against nanobacteria, a controversial, slow-growing, and calcifying microorganism. Therefore, experiments were designed to determine whether structures from aneurysms are viable, nano-sized organisms.
Methods: Aneurysms (n=3) collected as surgical waste were decalcified, sterile filtered (0.22 μm), and cultured in DMEM containing gamma-irradiated calf serum.
Results: In 2 of 3 cultures micron-sized particles visible by light microscopy increased in number over 4-6 weeks. The negative culture came from an aneurysm without stainable nanoparticles. With transmission electron microscopy (EM), cultured particles showed an inner core surrounded by a shell of calcium phosphate (documented via energy dispersive microanalysis). After dissolution of the shell with EDTA, spherical structures of 50-100 nm were seen by scanning EM. These cultured particles incorporated [^{3}H]uridine at a rate 2.3 times greater than control cultures of DMEM containing serum and inorganic hydroxyapatite (HA) crystals (P<0.01). Therefore, these nanostructures appear to synthesize RNA. Particles cultured from aneurysms also stained with the 8D10 antibody, and SDS-PAGE of extracted proteins revealed multiple distinct bands, including one (M_r 47 kDa) recognized by the 8D10 antibody. The pattern of proteins extracted from inorganic HA crystals incubated with DMEM and calf serum did not contain the 47-kDa band recognized by the 8D10 antibody.
Conclusion: In conclusion, these results suggest that viable nano-sized organisms are present within calcified human arterial tissue. A cause and effect relationship between the presence of these organisms and development of arterial calcification remains to be determined.

Noon

1059-14 C825T Polymorphism of the G-Protein Beta(3) Subunit Gene and Atrial Fibrillation: Association of the TT Genotype With a Reduced Risk for Atrial Fibrillation

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Background: A polymorphism consisting of a C825T substitution in the G-protein beta(3) subunit gene (GNB3) has been associated with enhanced signal transduction via heterotrimeric G-proteins. Furthermore, association between enhanced human atrial inward rectifier potassium currents and the TT genotype, but not the CT genotype has been shown. Therefore, we investigated a possible impact of the GNB3 C825T polymorphism on atrial fibrillation by genotyping patients with atrial fibrillation and a control cohort of patients without atrial tachyarrhythmias. Methods: 291 consecutive patients admitted to our center with symptomatic paroxysmal or persistent AF (mean age 58±10 years) and 292 control patients (59±11 years) were genotyped for the C825T polymorphism. Patients with coronary heart disease, valvular heart disease or cardiomyopathy were excluded from the study in order to avoid the influence of disease-related atrial remodeling. Control subjects were 292 consecutive patients admitted to our center in which coronary artery disease was excluded by coronary angiography. The control group had a similar incidence of cardiovascular risk factors (hypertension, hypercholesterolemia, body mass index) as the group with atrial fibrillation. Results: The prevalence of the GNB3 TT genotype was significantly lower in patients with atrial fibrillation (5.8%) than in the control group (12.0%); however, no significant differences in the frequencies of the CT and CC genotypes were found. TT genotype was associated with a 51% decrease in the unadjusted risk (OR: 0.49, 95% CI=0.28-0.85, P=0.01) and a 54% decrease in the adjusted risk (OR from a multivariant model: 0.46, 95% CI=0.24-0.87, P=0.02) for the occurrence of atrial fibrillation. Sinus cycle length, P wave duration, PQ interval and rate-corrected QT interval (QTc) during sinus rhythm were not influenced by the genotype. Conclusion: The present study suggests an association between the GNB3 TT genotype and a reduced risk for the occurrence of atrial fibrillation.

Noon

1059-15 Early Administration of Clopidogrel Is Safe After Off-Pump Coronary Artery Bypass Surgery

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Background: Patients who undergo off-pump coronary artery bypass (OPCAB) may be hypercoagulable with an increased risk of early graft thrombosis due to the lack of platelet dysfunction that accompanies “on-pump” coronary artery bypass. Clopidogrel, a

platelet aggregation inhibitor, is indicated in high risk cardiovascular patients to prevent recurrent ischemic events. Therefore, the purpose of this study was to determine the safety and efficacy of clopidogrel administration initiated in the early postoperative period after OPCAB.
Methods: 30-day follow-up of 364 OPCAB patients from Jan-June, 2001 was determined from prospectively collected data. 193 patients received clopidogrel approximately 4 hours postoperatively if chest tube output < 100cc/hr for 4 hours and then daily for 4-6 weeks. Telephone follow-up was made 6 – 12 months after OPCAB in 93% of clopidogrel and 88% of non-clopidogrel patients. Adverse cardiovascular events were defined as unstable angina, myocardial infarction, transient ischemic attack, or stroke.
Results: The 193 clopidogrel patients had significantly higher preoperative risk scores compared to the 171 non-clopidogrel patients: 3-vessel CAD, 62% vs. 50%, prior PTCA, 26% vs. 16%, prior intracoronary stent placement 19% vs. 7%, and CCS angina III-IV, 58% vs. 37%, p<0.02. None of the clopidogrel patients required reoperation for mediastinal hemorrhage. No group differences in mortality were observed at 6 months. For all risk categories, no differences in adverse cardiovascular events were observed, 3.4% of clopidogrel patients vs. 5.3% for non-clopidogrel patients, p=NS. However, in low risk patients (CCS angina score <2 and 1-2 vessel CAD), fewer adverse cardiovascular events occurred in the clopidogrel group, 1/92 (1.1%) vs. 6/73 (8.2%), p=0.045. Gastrointestinal bleeding occurred in 2.2% clopidogrel patients vs. 0.7% non-clopidogrel patients, p=NS.
Conclusions: According to this protocol, OPCAB patients can safely receive clopidogrel in the early postoperative period without increased risk for mediastinal hemorrhage. Early clopidogrel administration after OPCAB may be associated with a reduction in short-term adverse cardiovascular events.

Noon

1059-16 Can Autologous Myoblast Transplantation Decrease Chronic Ischemic Mitral Regurgitation?

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Background: Extensive work has confirmed the relationship between ischemic mitral regurgitation (MR) and remodeling of the infarcted left ventricle (LV), which displaces apically the papillary muscles to which the mitral leaflets are anchored. This study was thus designed to assess whether transplantation (Tx) of skeletal myoblasts could reduce mitral leaflet tethering and chronic ischemic MR by decreasing endsystolic volumes (ESV) and reshaping the infarcted wall. **Methods:** An open-chest infero-basal infarction was created in 14 sheep, thereby resulting in a MR which progressively developed over the ensuing 8 weeks. At this time point, sheep were randomly allocated to receive previously expanded autologous skeletal myoblasts (230 million cells, of which 65% were myoblasts identified by a positive staining for CD56, n = 7) or to serve as controls receiving culture medium only (n = 7). All injections were made in multiple sites in the infarcted posterior bulging wall. 3D echocardiography was used for serial evaluations performed immediately after infarction, 2 months therafter (preTx) and 2 additional months after Tx. End points included blinded measurements of the tethering distance between the ischemic medial papillary muscle tip and the anterior annulus, LV ejection fraction and stroke volume while 2D echo was used for assessing wall motion score (WMS). **Results:** Parameters (mean ± SEM) were similar at baseline and at 2 months between the 2 groups. Two months after Tx (i.e., 4 months post infarction), myoblast Tx was found to have reduced the progression of ischemic MR (regurgitation volume: 0.7 ± 0.5 *vs.* 5.7 ± 0.9 mL in controls, $p < 0.01$), the increase in ESV (30.4 ± 1.2 mL *vs.* 42.0 ± 2.8 mL in controls, $p < 0.01$) and the tethering distance (0.01 ± 0.05 cm *vs.* 0.44 ± 0.12 cm in controls, $p = 0.01$). The benefits of myoblast Tx were also evidenced by a lesser decrease of LV ejection fraction (2.9 ± 1.8% *vs.* 7.8 ± 1.9% in controls, $p < 0.01$) and a significant improvement of the WMS (-0.6 ± 0.03 *vs.* 0.1 ± 0.01, respectively, $p < 0.01$). **Conclusion:** Tx of skeletal myoblasts may attenuate mild to moderate chronic ischemic MR by decreasing ESV and reshaping the infarcted LV wall, thereby enhancing valve coaptation.

Noon

1059-17 Prolongation of Atrial Effective Refractory Period by Biatrial Subthreshold Stimulation

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Timely subthreshold atrial extrastimuli (AE) delivered in the refractory period can prevent the induction of atrial fibrillation (AF) by another AE delivered in the vulnerable period. This study aims to investigate the effect of subthreshold stimulation (SS) on atrial effective refractory period (AERP).
Methods: 14 patients without history of AF (9 male and 5 female, mean age of 51) were recruited. AERP of right atrial septum was determined after 5 minutes of pacing with 4 different protocols and 3 sets of cycle length (CL) commenced in random order with 10 minutes of washout time between each protocol. Protocols were as shown in table below, pacing at high right atrium (HRA) and bi-atrial (HRA + coronary sinus) was at twice diastolic threshold. SS was commenced by introduction of an electrical impulse of 2.0msec in duration and 20mA in amplitude at 50msec after the preceding captured pacing impulse. The mean of 3 AERP measurements was recorded.
Results: Analysis showed that the pacing protocol but not the CL had significant effect on AERP. Multiple comparisons showed that the Bi-atrial + SS group had significant longer AERP than all other groups (protocol 4 versus protocol 1, p< 0.001; versus protocol 2, p< 0.021; versus protocol 3, p< 0.002)

AERP±SD(msec)/ CL(msec)	HRA	HRA + SS	Bi-atrial	Bi-atrial +SS
600	218.2 ± 20.0	221.8 ± 20.8	216.8 ± 20.7	242.1 ± 31.8
500	218.6 ± 20.0	224.3 ± 22.2	220.0 ± 24.5	237.9 ± 30.7
400	211.1 ± 24.0	226.8 ± 20.0	225.4 ± 25.5	240.0 ± 32.3

Conclusion: Bi-atrial SS significantly prolonged AERP. It is plausible that because SS is relatively localized, the larger the area of atrium receives SS the greater its effect on AERP. The study result suggests that bi-atrial SS may be an effective therapy for prevention of AF.

Noon

1059-18 The Role of Slow Delayed Rectifier Potassium Current (I_{Ks}) in Cardiac Electrophysiology and Atrial Fibrillation

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Background: The role of I_{Ks} in cardiac electrophysiology has been controversial: direct experimental analysis has been limited by a lack of adequate probes. In this study, we used a highly-selective I_{Ks} blocker, HMR1556 (HMR), to evaluate the I_{Ks} contribution to cardiac electrophysiological function and AF maintenance.
Methods: Anesthetized open-chest dogs were studied before and after HMR alone (1 mg/kg IV), HMR plus nadolol 0.5 mg/kg IV, dofetilide alone (D, 0.16 mg/kg IV) or HMR plus D (H/D).
Results: HMR alone increased atrial (AERP at cycle length, CL, 300 ms, $AERP_{300}$: 88±11, M±SD, to 105±13 ms, *p<.05) and ventricular ($VERP_{600}$: 154±14 to 190±32 ms*) effective refractory period with positive or no frequency-dependence, and increased sinus node recovery time (SNRT). Beta blockade eliminated HMR effects on AERP ($AERP_{300}$: 99±5 to 101±17 ms) and SNRT, but did not alter changes in VERP ($VERP_{600}$: 177±19 to 211±11 ms*). D prolonged both AERP ($AERP_{300}$: 92±4 to 143±17 ms*) and VERP ($VERP_{600}$: 179±18 to 213±29 ms*) with reverse use dependence. In the presence of D, HMR effects were significantly increased, e.g. HMR increased $AERP_{300}$ 22±10% vs control, H/D increased $AERP_{300}$ 29±12%* vs D; HMR increased $VERP_{600}$ 24±19% vs control, H/D increased $VERP_{600}$ 32±5%* vs D. In addition, Wenckebach CL was not affected by HMR alone, but was greatly increased by H/D vs D alone. HMR shortened the duration of induced vagotonic AF (DAF, 1077±198 to 471±339 sec*), an effect abolished by β-blockade. D had no significant effect on DAF (916±216 to 732±243 ms), but H/D markedly decreased DAF (to 77±73 ms, p<.001).
Conclusions: I_{Ks} plays a role in baseline atrial, ventricular and SA node repolarization in vivo, with atrial and SA nodal effects being dependent on background β-adrenoceptor stimulation. I_{Ks} also plays a role in AF maintenance in the presence of intact sympathetic tone. I_{Ks} effects are particularly important in the presence of reduced repolarization reserve, as indicated by the synergistic interaction between HMR and D. This constitutes the first evaluation of the role of I_{Ks} for in vivo cardiac electrophysiology and highlights the distinct profile of I_{Ks} vs I_{Kr} blockade.

Noon

1059-19 Effect of Cardiac Resynchronization Therapy in Patients With Right Bundle Branch Block

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Background: Cardiac resynchronization therapy (CRT) is indicated for pts with heart failure and QRS delay. There is no published data evaluating CRT in pts with right bundle branch block (RBBB). Methods: Data was analyzed at baseline and 6 months in the 501 pts with NYHA FC II-IV heart failure and ICD indications enrolled in the CONTAK CD Trial (Guidant, Corp). Results: A total of 66/501 (13%) pts had RBBB, 271/501 (62%) had LBBB and 164/501 (38%) had IVCD. There were no differences in baseline characteristics between RBBB and non-RBBB pts. Unlike non-RBBB pts, RBBB pts did not demonstrate improvement in symptom status, heart size or LVEF (Table). NYHA FC did not improve with RBBB pts and the subset of enrolled pts with FC III-IV symptoms also showed no benefit. Conclusion: CRT may not benefit RBBB pts. A meta-analysis of the completed controlled trials of RBBB pts is needed to corroborate these findings. Alternative stimulation sites should be tested in this subset.

Table

Endpoint	Time	RBBB CRT/No CRT, p	Non RBBB CRT/No CRT, p
V02 (ml/kg/min)	Baseline 6 mo change	13±.5/13±.5 -1±.6/-.1±.6, ns	14±.2/14±.2 1±.3/0±.3, .009
6 min walk (m)	Baseline 6 mo change	302±14/302±13 10±18/21±17, ns	320±6/320±6 39±8/13±8, .02
LVIDs (sys/mm)	Baseline 6 mo change	54±1/54±1 -1±2/-2±2, ns	59±.5/59±.5 59±.5/59±.5 -4±.7/-.6±.7, < .001
LVEF (%)	Baseline 6 mo change	31±1/31±1 2±2/4±1, ns	27±.4/27±.4 6±.8/3±.8, .008